Clinical review

Panic disorder

C Barr Taylor

Panic disorder, with or without agoraphobia, is one of the most common and important anxiety disorders in the general population in the Western world with a prevalence in one year of 2-3% in Europe.[1] Agoraphobia without panic occurs in another 1% of the population. Patients with panic disorder have a high use of medical services, an impaired social and work life, and an overall reduced quality of life.[2 3] The good news is that short term, psychological interventions can improve the lives of most patients. Protocols and resources to help general practitioners implement such techniques, with and without drugs, are available.

Summary points

- Patients with panic disorder should be offered psychotherapy, drugs, and self help
- Patients with panic disorder must be carefully assessed for depression and suicidal tendency
- Cognitive behaviour therapy (face to face or through internet based programs) can reduce the frequency of panic attacks and avoidance behaviour in most patients; psychoeducation and self help may be sufficient to treat uncomplicated cases with recent onset
- Selective serotonin reuptake inhibitors are the drug of choice, but if they are not suitable or no improvement is seen after a 12 week course, imipramine or clomipramine should be considered
- Benzodiazepines should be used only when symptoms are incapacitating and only for a short time
- Patients' preferences should be taken into account when determining which treatments to offer

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BMJ 2006;332:951–5

Sources and selection criteria

This review is based on searches in PubMed for meta-analyses of the efficacy of treatment of panic disorder, including the National Institute for Health and Clinical Excellence (NICE) clinical guideline for anxiety and panic disorder (guideline 22).[4]

What is panic disorder?

The main feature of panic disorder is recurrent, unexpected panic attacks. Most patients with the disorder avoid situations where they think a panic attack may occur, and avoidance may severely limit their life. Agoraphobia can occur without panic attacks, although patients may have episodes such as gastrointestinal distress and diarrhoea that are equivalent to panic attacks. Most of the evidence based studies on panic disorder and agoraphobia use the DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders*, fourth edition) criteria (box). However, many practitioners use ICD-10 (International Classification of Diseases, 10th revision), which states that the "essential feature is recurrent attacks of severe anxiety (panic), which are not restricted to any particular situation or set of circumstances and are therefore unpredictable."

What other psychiatric conditions are associated with panic?

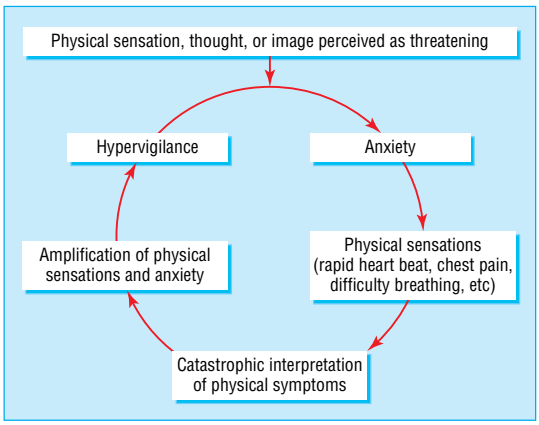
Panic disorder is associated with several psychiatric conditions, such as depression and other anxiety disorders.[5] About a third of patients with depression present with panic disorder. Over a lifetime, about half of patients with panic disorder will develop depression and about half of depressed patients will develop panic disorder. Patients may misuse alcohol or drugs (or both) to cope with panic, and, in turn, the use of these substances may unleash panic disorder. Importantly, the risk of suicide is raised in patients with panic disorder, especially those with comorbid depression.[6] A recent study in the United States found a sevenfold increase in suicidal thoughts in patients with panic and depression.[7]

What medical conditions occur with panic attacks?

Panic disorder has been associated with many medical disorders, including mitral valve prolapse, migraine headaches, asthma, vestibular abnormalities, and hypertension. It is not known whether these associations are an artefact of the health seeking behaviour of such patients or true comorbid conditions. Older patients with panic disorder and avoidance may have an increased risk of cardiovascular mortality.[8] The reason for this is unclear.

What causes panic disorder?

The cause of panic disorder is unknown. Several factors probably contribute to its development, and no biological test is available. Genetic and early family factors, or both, are important. Gorman et al argue that patients inherit a sensitive "central nervous system fear mechanism, centered in the amygdala" although several other brain areas are also implicated.[9] A psychological model suggests that panic attacks and panic disorder represent "fear of fear."[10] In this model (figure), physical sensations associated with anxiety—feeling dizzy or faint, or having a pounding heart, shortness of breath, or chest pain—are interpreted as indicating a dire consequence (I am going to faint, have a heart attack, not be able to breathe). This leads to hypervigilance about bodily sensations, increased arousal of the sympathetic nervous system, more physical sensations, and heightened anxiety, which spirals into a panic attack.



Cognitive model of panic: symptoms, hypervigilance, and anxiety spiral into panic attack. Patients develop "fear of fear" and avoid situations where they think they will have a panic attack

Panic disorder can be caused by traumatic events, excessive caffeine, and misuse or withdrawal of drugs or alcohol. Evidence that hyperventilation causes panic attacks is conflicting.[11] Chronic hyperventilation should lead to hypocapnia, but the partial pressure of carbon dioxide when resting is similar in patients with panic disorder and controls. In the laboratory, prolonged hyperventilation can produce panic attacks.

American Psychiatric Association DSM-IV criteria for panic disorder and agoraphobia

Panic attack (not a DSM-IV code)

A discrete period of intense fear or discomfort in which four (or more) of the following symptoms developed abruptly and reached a peak within 10 minutes:

- Palpitations, pounding heart, or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or smothering
- Sensation of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, light headed, or faint
- Derealisation (feelings of unreality) or depersonalisation (being detached from oneself)
- Fear of losing control or going crazy
- Fear of dying
- Paraesthesias
- Chills or hot flashes

Agoraphobia (not a DSM-IV code)

- Anxiety about being in places or situations from which escape is difficult (or embarrassing) or in which help may not be available. Consider the diagnosis of a specific phobia if avoidance is limited to one or a few specific situations, or social phobia if avoidance is limited to social situations
- The situations are avoided or endured with great distress or anxiety about having a panic attack

Panic disorder without agoraphobia (300.01)

- Recurrent, unexpected panic attacks, one of which at least is followed by one month (or more) of at least one of:
  - Persistent concern about having additional attacks
  - Worry about the implications of the attack or its consequences
  - A significant change in behaviour related to the attacks
- Panic attacks are not due to drug misuse, prescribed drugs, or a medical condition
- The panic attacks are not better accounted for by another disorder
- Absence of agoraphobia (see below)

Panic disorder with agoraphobia (300.21)

Characterised by the above criteria for panic disorder but with agoraphobia:

- Anxiety about being in places or situations from which escape might be difficult (or embarrassing)
- Avoiding these situations or enduring them with great distress or anxiety

Agoraphobia without history of panic disorder (300.22)

Characterised by the criteria for agoraphobia but not panic disorder

How is panic disorder diagnosed?

The diagnosis of panic disorder is relatively straightforward. However, distinguishing panic attacks from medical disorders is difficult because symptoms that occur with panic attacks cover a wide range of medical problems. For example, about a quarter of patients who present with chest pain have panic disorder. In most of these patients, chest pain during the panic attack is not related to cardiac problems, but some may have panic attacks during times of myocardial ischaemia and the symptoms are similar. A careful history can usually lead to a diagnosis of panic disorder. Diseases that can cause panic disorder, such as hyperthyroidism, need to be ruled out. Panic disorder should be a positive diagnosis and not one of exclusion.

How are panic attacks treated?

Standard treatments are psychoeducation, psychotherapy (particularly cognitive behaviour therapy), lifestyle changes, and drugs (alone or combined). NICE guideline 22 concludes that psychotherapy, drugs, and self help (bibliotherapy) are effective and should be offered to patients, and patients' preferences and experience with previous treatment(s) should be taken into account. Patients, families, and care givers should be informed of self help groups and support groups and encouraged to participate in such programmes if appropriate.

GP tips

- Treat panic disorder and agoraphobia with cognitive behaviour therapy, drugs, and self help (bibliotherapy)
- Ensure that cognitive behaviour therapy and self help are available to patients. Identify qualified local practitioners of cognitive behaviour therapy or register the patient on FearFighter (an internet based program for treating panic), or both. Licences to use FearFighter are available for general practices (stuart@ccbt.co.uk)
- Monitor symptoms and progress, especially the frequency and severity of panic attacks and avoidance. Treatment should prevent panic attacks and avoidance
- A selective serotonin reuptake inhibitor should be the first drug of choice; warn patients of potential side effects (including transient increase in anxiety at the start of treatment) and the risk of symptoms when the drug is stopped
- If the patient does not improve in 12 weeks, consider another class of antidepressant or another form of treatment (such as cognitive behaviour therapy)
- Offer referral to a mental health specialist if the patient still has appreciable symptoms after two types of treatment have been provided
- Warn patients that relapse is likely and to contact you if symptoms recur

What is the role of psychoeducation and self help?

Educating patients about the nature of panic disorder can be helpful and may be sufficient for patients without complications, although this assumption has not been tested in controlled studies. The basic information can be presented in a handout, or patients can be referred to self help and internet resources.

What is the role of lifestyle management?

Patients should be encouraged to reduce caffeine intake, and sources of caffeine in the diet should be explained. Muscle relaxation techniques are useful and can be taught by using tapes or CDs, but relaxation proved less effective than behavioural and cognitive therapies in controlled trials. Exercise is often recommended to expose patients to increased heart rate and shortness of breath, but it has not been evaluated in controlled studies. Stress management might be helpful, but it has not been systematically evaluated.

How effective is cognitive behaviour therapy?

Cognitive behaviour therapy comprises several cognitive and behavioural procedures. The behaviour part is usually "exposure"—people are encouraged to experience or encounter their feared situations or sensations under conditions of perceived safety. The rationale for this treatment derives from studies of fear habituation in animals. More recently, exposure therapy has been expanded to focus on real life situations or stimuli and the response to internal cues, such as high heart rate, hyperventilation, and dizziness. For example, a patient with fear of a pounding heart may be asked to run on the spot in the doctor's office while paying attention to and reconsidering anxieties, such as "My heart rate is very fast, I am going to die."

A recent large, international, controlled study found that brief cognitive behaviour therapy (six to eight hours of therapy, supplemented with hand held computers or manuals) relieved panic attacks for most patients and was as effective as longer treatments.[12] NICE guideline 22 recommends seven to 14 hours of cognitive behaviour therapy—usually weekly sessions of one to two hours, completed within four months.[4]

Retraining in breathing—where patients are taught to breathe slower, deeper, and more regularly—is a core feature of most psychological treatments for panic disorder, although its effectiveness is unconfirmed.

Cognitive behaviour therapy needs to deal with the cognitive aspects of panic and avoidance behaviour. Many patients who seem to be functioning well avoid activities that may hamper their performance, such as crossing bridges, making public presentations, or attending group meetings. Patients with panic disorder may develop elaborate ways of disguising their problems.

What is the role of drugs?

Antidepressants are the first line drug for patients with panic disorder: selective serotonin reuptake inhibitors are recommended because they are effective and have few side effects. Few studies have shown differences between these inhibitors, and newer inhibitors are probably no more or less effective than older ones. Some patients experience restlessness, sweating, and tachycardia (jitteriness syndrome) when they start taking antidepressants. This might be avoided by starting at lower than usual doses. The effects of stopping these drugs may be especially upsetting to some patients with panic disorder, but the effects can be minimised by discontinuing the drugs over several weeks. Although these drugs are not associated with tolerance and craving, discontinuation or withdrawal symptoms may occur when the drug is stopped or doses are missed or, occasionally, when the dose is reduced. These symptoms are usually mild and self limiting but occasionally can be severe, especially if the drug is stopped abruptly.

Unanswered research questions

- How effective are combinations of treatment (for example, combinations of drugs, combinations of drugs and psychotherapy)?
- Should cognitive behaviour therapy automatically be combined with drugs?
- What are the most cost effective treatments and how can they be made more cost effective?
- How long should drugs be used for?
- What factors can predict response and relapse? How can response rates be improved and relapse rates reduced?
- How effective are new antidepressants?
- How do comorbid conditions (such as depression and substance misuse) affect outcome and how should such conditions be treated?

Also see www.rcgp.org.uk/nccpc (CG22 Anxiety. Full guideline, section 12, pp 152-3)

Evidence for the effectiveness of other drugs is less compelling. NICE guideline 22 concludes that, "sedating antihistamines or antipsychotics should not be prescribed in the treatment of panic disorder." Imipramine and chlomipramine are efficacious. Preliminary evidence shows that some of the newer antidepressants may also be effective.

Benzodiazepines can be effective for treating panic disorder, but their use is controversial because of potential dependence, drowsiness, and impaired concentration. Benzodiazepines may interfere with the efficacy of cognitive behaviour therapy. It may be difficult to withdraw patients from benzodiazepines, so they should be used sparingly. However, for patients with severe panic or in whom avoidance causes considerable work, family, or social problems, short term use of benzodiazepines may be indicated until psychological approaches and other drugs start to work. Some patients like to keep a "pill in their pocket" as a safety measure, although some clinicians argue that until such "props" are eliminated the patient cannot recover fully. NICE guideline 22 concludes that, "benzodiazepines are associated with a worse outcome in the long term and should not be prescribed in the treatment of individuals with panic disorder."

Some studies indicate that drugs should be combined with psychotherapy,[13 14] although the patient's preference and the availability of experienced therapists need to be considered. This combination leads to better short term outcomes, facilitates stopping drugs, and prevents relapse once drugs have been stopped.

It is unclear how long drugs should be taken for. A common rule is that they should be taken until patients are panic-free for at least six months and non-avoidant, but many patients function well with infrequent or partial panic attacks. Patients with depression may be at greater risk of relapse, and they may need longer periods of drug treatment than patients without depression. Withdrawing or stopping the drug when the patient is in psychotherapy has advantages—it may increase the benefit of therapy as patients cannot attribute success to the use of drugs.

Information sources for patients

Internet resources

American Psychiatric Association (http://www.apa.org/topics/anxietyqanda.html)—This website explains the causes, symptoms, and treatment of panic disorders

National Institute of Mental Health (www.nimh.nih.gov/healthinformation/panicmenu.cfm?)—This website provides information on panic attacks, including a fact sheet and an easy to read booklet

The Open-Mind (www.open-mind.org/SP/Help/index.htm)—This website provides a summary of self help books, newsgroups, and organisations in the UK, US, Canada, and many other countries with a focus on the treatment of anxiety disorders

The Anxiety Association of America (www.adaa.org)—This website provides information on anxiety disorders and how to get help

The National Phobics' Society (www.phobics-society.org.uk)—Website of a charity devoted to helping people with anxiety disorders, including panic disorder

Self help books

Barlow DH, Craske MG. *Mastery of your anxiety and panic (MAP-3). Client workbook for anxiety and panic.* 3rd ed. Oxford: Oxford University Press, 2000—This book has been used successfully in evidenced based trials

Bourne EJ. *The anxiety and phobia workbook.* 4th ed. Oakland, CA: New Harbinger Press, 2005—A very popular book, but its effectiveness has not been evaluated in clinical trials

Marks IM. *Living with fear.* 2nd ed. London: McGraw-Hill—Use of the book was effective as bibliotherapy in a randomised trial

Information sources for practitioners

BMJ Publishing Group. *Clinical evidence: panic disorder.* (www.clinicalevidence.org/ceweb/conditions/meh/1010/1010.jsp)

Mitte K. A meta-analysis of the efficacy of psycho- and pharmacotherapy in panic disorder with and without agoraphobia. *J Affect Disord* 2005;88:27-45

Otto KW, Powers M, Smits JAJ. Adding cognitive-behavioral therapy to pharmacotherapy for panic disorder: issues and strategies. *CNS Spectr* 2005:9(suppl 12):32-9

Also see references 4, 13, 16, and 17

Are patients likely to relapse?

Many patients who are successfully treated for panic will have panic attacks some time in the future. This can be discouraging to patients, so they should be told that relapse may occur and that they should not fall into bad habits (such as avoidance or catastrophic thoughts). They should be encouraged to come in for a consultation to see whether a refresher course of cognitive behaviour therapy or restarting drugs might help.

What if psychoeducation, brief therapy, and drugs do not work?

Some patients with panic disorder and agoraphobia still have symptoms after standard treatment. When initial treatment fails, other antidepressants or combinations of drugs should be tried, and cognitive behaviour therapy should be given if it has not already been used.[15] Algorithms and treatment guidelines for drug use with panic disorder are available.[11 16 17] NICE guideline 22 recommends that if no improvement is seen after a 12 week course, imipramine or clomipramine should be considered. If the patient still has severe symptoms after two interventions, the guideline recommends referral to a specialist in mental health.

Can the internet help treat panic disorder?

Given the effectiveness of cognitive behaviour therapy for panic attacks, it is not surprising that psychotherapy programs for panic have been developed for hand held computers and the internet. In a review of cognitive behaviour treatment for anxiety, NICE guideline 97 recommends FearFighter, an internet based program, as an option for delivering cognitive behaviour therapy for the management of panic and phobia.[18]

How can panic disorder be managed in primary care?

The effectiveness of cognitive behaviour therapy and drug treatment and the need to develop treatment approaches for general practice have generated several practice based and system based protocols.

One study randomised 232 primary care patients to usual care or an intervention comprising a combination of up to six sessions (across 12 weeks) of cognitive behaviour therapy modified for the primary care setting, with up to six follow-up telephone contacts during the next nine months, and algorithm based drug treatment provided by the primary care doctor with guidance from a psychiatrist.[19] The combined psychotherapy and drug intervention was most effective.

Another study randomised primary care patients with panic disorder to a case management model of usual care.[20] The case manager provided psychoeducation and treatment recommendations (self help, referral, drugs) via the telephone. Compared with usual care, the intervention group had a significant reduction in panic symptoms. A study in Amsterdam compared the effectiveness of general practitioners who provided self help or cognitive behaviour therapy according to structured guidelines with psychotherapy carried out by professionals in mental health.[21] All three forms of treatment produced a significant improvement, which remained stable at follow-up. This study showed that general practitioners can provide effective cognitive behaviour therapy. NICE guideline 22 notes that cognitive behaviour therapy should be delivered only by suitably trained and supervised people who adhere closely to empirically grounded treatment protocols.

Competing interests: None declared.

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(Accepted 8 March 2006)

Letter home

Hi Mom and Dad,

I hope you are well there and I am also well (in this hell). I am writing to you after a long time as I was very busy in my work (applying for clinical attachments). You should not worry about me (as I am already worried about myself). The place where I am putting up (East Ham) is just like India. I have got one room shared by 6 people, very comfortable (for cockroaches and mosquitoes). There are lots of Indians in this area (as Britishers do not like to come here) and most are doctors like me (PLABers, or one can say beggars).

Mamma, I have changed a lot and you may not believe me but I go to a temple and a gurudwara daily (to have my lunch and dinner). Dad, you used to worry that I will be drinking a lot here, but let me tell you that I have not touched liquor and have even stopped taking tea (as I can't afford this luxury). You teased me that I will be running after girls here, but I am not running after females (as most of the time I am sending emails). I have travelled to a lot of places now, and it's difficult to remember each place (where I tried so hard for a clinical attachment). You will be surprised that I do not watch any TV (as every day I am changing my CV). You used to say that I just sit at home and eat all the time; now I jog 5-10 miles daily (as I can't afford buses and taxis). And, Mamma, your son has lost 10 kg and become much smarter.

They will be paying a handsome salary during my clinical attachment (I have to give them £100 to get it and £200 for board and lodging). You will be glad to know that I am thinking of some side business in the financial sector, like how to generate money (borrowing from friends, in debt for PLAB-II coaching).

I really miss you so much, and sometimes I think of coming back to you, leaving all these luxuries behind (which I will have to if I can't find £500 for a visa extension). I asked you to get your passports ready, but I think that you should wait, as here the weather is not conducive for elderly parents. Mamma, I request you that you should also go to gurudwara daily and make some donations (as your son is surviving at the mercy of these temples).

I will write to you again as I am about to finish my time for using the computer.

your son.

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I thank Dr Vinita Kumari for helping me to write this article.